

**IN THE CLAIMS (37 CFR 1.121 Revised)**

1. (original) A pharmaceutical composition comprising a combination of an inverse agonist of the GABA<sub>A</sub>  $\alpha$ 5 receptor subtype; a nicotine receptor partial agonist (NRPA), estrogen, selective estrogen modulators, or vitamin E; and a pharmaceutically acceptable carrier.

2. (original) The pharmaceutical composition of claim 1, wherein the inverse agonist has a functional efficacy at the  $\alpha$ 5 receptor subtype of less than 20%, and a functional efficacy at the  $\alpha$ <sub>1</sub>,  $\alpha$ <sub>2</sub> and  $\alpha$ <sub>3</sub> receptor subtypes of between -20 and +20%.

3. (currently amended): A pharmaceutical composition comprising a combination of an inverse agonist of a GABA  $\alpha$ 1 and/or  $\alpha$ 5 receptor subtype; a nicotine receptor partial agonist (NRPA), estrogen, selective estrogen modulators, or vitamin E; and a pharmaceutically acceptable carrier; wherein the GABA<sub>A</sub> inverse agonist has a functional efficacy at the  $\alpha$ 1 and/or  $\alpha$ 5 receptor subtypes of less than -5%~~[-preferably less than -10%]~~ and the efficacy measured at the  $\alpha$ 2 and  $\alpha$ 3 receptor subtypes is greater than 5%~~[-or preferably greater than 10%]~~.

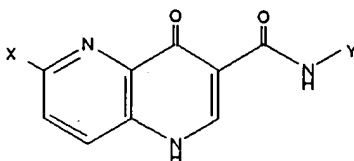
4. (currently amended): The pharmaceutical composition of claim 3, wherein the GABA<sub>A</sub> inverse agonist has functional potency (EC<sub>50</sub> values) at the  $\alpha$ 1 and/or  $\alpha$ 5 receptor subtypes of 200 nM~~[-preferably less than 150 nM]~~.

5. (currently amended): The pharmaceutical composition of claim 3, wherein the GABA<sub>A</sub> inverse agonist has a functional efficacy at the  $\alpha$ 5 receptor subtype of less than -5%~~[-preferably less than -10%]~~, and the efficacy measured at the  $\alpha$ 1,  $\alpha$ 2 and  $\alpha$ 3 receptor subtypes is greater than 5%~~[-or preferably greater than 10%]~~.

6. (currently amended): The pharmaceutical composition of claim 5 wherein the GABA<sub>A</sub> inverse agonist has a functional potency (EC<sub>50</sub> values) at the  $\alpha$ 5 receptor subtype of 200 nM~~[-preferably less than 150 nM]~~.

7. (currently amended): The pharmaceutical composition of claim 3 wherein the GABA<sub>A</sub> inverse agonist at the  $\alpha$ 1 and/or  $\alpha$ 5 receptor subtypes has a binding K<sub>i</sub> of 100 nM~~[-preferably less than 30 nM]~~.

8. (currently amended): The pharmaceutical composition of claim 1, wherein the GABA<sub>A</sub> inverse agonist is selected from a compound of Formula I :



wherein:

X is hydrogen, halogen, -OR<sub>1</sub>, NR<sub>2</sub>R<sub>3</sub>, C<sub>1</sub>-C<sub>6</sub> alkyl optionally substituted with up to three groups selected independently from halogen and hydroxy, or -NR<sub>2</sub>R<sub>3</sub>; or

X is phenyl, naphthyl, 1-(5,6,7,8-tetrahydro)naphthyl or 4-(1,2-dihydro)indenyl, pyridinyl, pyrimidyl, isoquinolinyl, 1,2,3,4-tetrahydroisoquinolinyl, benzofuranyl, benzothienyl, each of which is optionally substituted with up to three groups selected from halogen, C<sub>1</sub>-C<sub>6</sub> alkyl, C<sub>1</sub>-C<sub>4</sub> alkoxy, C<sub>1</sub>-C<sub>6</sub> alkylthio, hydroxy, amino, mono or di(C<sub>1</sub>-C<sub>6</sub>) alkylamino, cyano, nitro, trifluoromethyl; or

X represents a carbocyclic group herein termed [{"the X carbocyclic group"}] containing from 3 - 7 [~~members~~] atoms, up to two of which are optionally hetero atoms selected from oxygen and nitrogen, where the X carbocyclic group is optionally substituted with one or more groups selected from halogen, (C<sub>1</sub>-C<sub>6</sub>)alkoxy, mono- or di(C<sub>1</sub>-C<sub>6</sub>)alkylamino, sulfonamide, aza(C<sub>3</sub>-C<sub>7</sub>)cycloalkyl, (C<sub>3</sub>-C<sub>7</sub>)cycloalkylthio, (C<sub>1</sub>-C<sub>6</sub>)alkylthio, phenylthio, or a heterocyclic group; and

Y is lower alkyl having 1 - 8 carbon atoms optionally substituted with up to two groups selected from halogen, (C<sub>1</sub>-C<sub>6</sub>)alkoxy, mono- or di(C<sub>1</sub>-C<sub>6</sub>)alkylamino, sulfonamide, aza(C<sub>3</sub>-C<sub>7</sub>)cycloalkyl, (C<sub>3</sub>-C<sub>7</sub>)cycloalkylthio, (C<sub>1</sub>-C<sub>6</sub>)alkylthio, phenylthio, a heterocyclic group, -OR<sub>4</sub>, -NR<sub>5</sub>R<sub>6</sub>, SR<sub>7</sub>, or aryl; or

Y is a carbocyclic group herein termed [{"the Y carbocyclic group"}] having from 3 - 7 [~~members~~] atoms, where up to three of which are optionally hetero atoms selected from oxygen and nitrogen and where any member of the Y carbocyclic group is optionally substituted with halogen, -OR<sub>4</sub>, -NR<sub>5</sub>R<sub>6</sub>, SR<sub>7</sub>, aryl or a heterocyclic group; and

R<sub>1</sub> is hydrogen, lower alkyl having 1 - 6 carbon atoms, or cycloalkyl having 3 - 7 carbon atoms, wherein each lower alkyl may be optionally substituted with -OR<sub>4</sub> or -NR<sub>5</sub>R<sub>6</sub>;

R<sub>2</sub> and R<sub>3</sub> are the same or different and represent hydrogen, lower alkyl optionally mono- or disubstituted with alkyl, aryl, halogen, or mono- or di-lower alkyl; aryl or aryl (C<sub>1</sub>-C<sub>6</sub>)alkyl where each aryl is optionally substituted with up to three groups selected from halogen, hydroxy, C<sub>1</sub>-C<sub>6</sub> alkyl, C<sub>1</sub>-C<sub>6</sub> alkoxy, or mono- or di(C<sub>1</sub>-C<sub>6</sub>)alkylamino;

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cycloalkyl having 3 – 7 carbon atoms optionally mono or disubstituted with halogen, alkoxy, or mono- or di- lower alkyl; or

-SO<sub>2</sub>R<sub>8</sub>;

R<sub>4</sub> is as defined for R<sub>1</sub>;

R<sub>5</sub> and R<sub>6</sub> carry the same definitions as R<sub>2</sub> and R<sub>3</sub>, respectively;

R<sub>7</sub> is hydrogen, lower alkyl having 1 – 6 carbon atoms, or cycloalkyl having 3 – 7 atoms; and

R<sub>8</sub> is lower alkyl having 1 – 6 carbon atoms, cycloalkyl having 3 – 7 carbon atoms, or optionally substituted phenyl;

or an isomer or hydrate thereof, or a pharmaceutically acceptable salt thereof.

9. (original) The pharmaceutical composition of claim 1, wherein the GABA<sub>A</sub> inverse agonist is selected from the group consisting of:

N-n-Butyl-6-chloro-4-oxo-1,4-tetrahydro-1,5-naphthyridine-3-carboxamide;

N-n-Butyl-6-ethoxy-4-oxo-1,4-tetrahydro-1,5-naphthyridine-3-carboxamide;

N-(2-Ethylthio)ethyl-6-methoxy-4-oxo-1,4-tetrahydro-1,5-naphthyridine-3-carboxamide;

N-n-Pentyl-6-ethoxy-4-oxo-1,4-tetrahydro-1,5-naphthyridine-3-carboxamide;

N-Benzyl-6-ethoxy-4-oxo-1,4-tetrahydro-1,5-naphthyridine-3-carboxamide;

N-(2-Tetrahydrofuranyl)methyl-6-ethoxy-4-oxo-1,4-tetrahydro-1,5-naphthyridine-3-carboxamide;

N-Isoamyl-6-ethoxy-4-oxo-1,4-tetrahydro-1,5-naphthyridine-3-carboxamide;

N-(3-Methoxybenzyl)-6-ethoxy-4-oxo-1,4-tetrahydro-1,5-naphthyridine-3-carboxamide;

N-(3-Ethoxy)propyl-6-ethoxy-4-oxo-1,4-tetrahydro-1,5-naphthyridine-3-carboxamide;

N-2-(2-Methyl)butyl-6-ethoxy-4-oxo-1,4-tetrahydro-1,5-naphthyridine-3-carboxamide;

N-5-Pentanol-6-ethoxy-4-oxo-1,4-tetrahydro-1,5-naphthyridine-3-carboxamide;

N-Benzyl-6-methoxy-4-oxo-1,4-tetrahydro-1,5-naphthyridine-3-carboxamide;

N-(2-Fluorobenzyl)-6-methoxy-4-oxo-1,4-tetrahydro-1,5-naphthyridine-3-carboxamide;

N-(3-Fluorobenzyl)-6-methoxy-4-oxo-1,4-tetrahydro-1,5-naphthyridine-3-carboxamide;

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N-(4-Fluorobenzyl)-6-methoxy-4-oxo-1,4-tetrahydro-1,5-naphthyridine-3-carboxamide;

N-(4/5-Imidazolyl)methyl-6-ethoxy-4-oxo-1,4-tetrahydro-1,5-naphthyridine-3-carboxamide;

N-(3-Thienyl)methyl-6-ethoxy-4-oxo-1,4-tetrahydro-1,5-naphthyridine-3-carboxamide;

N-(2-Tetrahydropyranyl)methyl-6-ethoxy-4-oxo-1,4-tetrahydro-1,5-naphthyridine-3-carboxamide;

N-(2-Fluorobenzyl)-6-ethoxy-4-oxo-1,4-tetrahydro-1,5-naphthyridine-3-carboxamide;

N-(3,5-Fluorobenzyl)-6-ethoxy-4-oxo-1,4-tetrahydro-1,5-naphthyridine-3-carboxamide;

N-(4-Fluorobenzyl)-6-ethoxy-4-oxo-1,4-tetrahydro-1,5-naphthyridine-3-carboxamide;

N-(4-Methoxybenzyl)-6-ethoxy-4-oxo-1,4-tetrahydro-1,5-naphthyridine-3-carboxamide;

N-(4-Methylbenzyl)-6-ethoxy-4-oxo-1,4-tetrahydro-1,5-naphthyridine-3-carboxamide;

N-(2-Thienyl)methyl-6-(2-methoxyethoxy)-4-oxo-1,4-tetrahydro-1,5-naphthyridine-3-carboxamide;

N-(2-Thienyl)methyl-6-morpholino-4-oxo-1,4-tetrahydro-1,5-naphthyridine-3-carboxamide;

N-(2-Thienyl)methyl-6-dimethylamino-4-oxo-1,4-tetrahydro-1,5-naphthyridine-3-carboxamide;

N-(4-Methylaminomethyl)benzyl-6-ethoxy-4-oxo-1,4-tetrahydro-1,5-naphthyridine-3-carboxamide;

N-(3-Methylaminomethyl)benzyl-6-ethoxy-4-oxo-1,4-tetrahydro-1,5-naphthyridine-3-carboxamide hydrochloride; and

N-[4-(Imidazolylmethyl)benzyl]-6-ethoxy-4-oxo-1,4-tetrahydro-1,5-naphthyridine-3-carboxamide.

10. (original) The pharmaceutical composition of claim 1 in which the NRPA is selected from the group consisting of:

9-bromo-1,2,3,4,5,6-hexahydro-1,5-methano-pyrido[1,2-a][1,5]diazocin-8-one;

9-chloro-1,2,3,4,5,6-hexahydro-1,5-methano-pyrido[1,2-a][1,5]diazocin-8-one;

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9-flouro-1,2,3,4,5,6-hexahydro-1,5-methano-pyrido[1,2-a][1,5]diazocin-8-one;  
9-ethyl-1,2,3,4,5,6-hexahydro-1,5-methano-pyrido[1,2-a][1,5]diazocin-8-one;  
9-methyl-1,2,3,4,5,6-hexahydro-1,5-methano-pyrido[1,2-a][1,5]diazocin-8-one;  
9-phenyl-1,2,3,4,5,6-hexahydro-1,5-methano-pyrido[1,2-a][1,5]diazocin-8-one;  
9-vinyl-1,2,3,4,5,6-hexahydro-1,5-methano-pyrido[1,2-a][1,5]diazocin-8-one;  
9-bromo-3-methyl-1,2,3,4,5,6-hexahydro-1,5-methano-pyrido[1,2-a][1,5]diazocin-8-one;  
3-benzyl-9-bromo-1,2,3,4,5,6-hexahydro-1,5-methano-pyrido[1,2-a][1,5] diazocin-8-one;  
3-benzyl-9-chloro-1,2,3,4,5,6-hexahydro-1,5-methano-pyrido[1,2-a][1,5] diazocin-8-one;  
9-acetyl-1,2,3,4,5,6-hexahydro-1,5-methano-pyrido[1,2a][1,5]diazocin-8-one;  
9-iodo-1,2,3,4,5,6-hexahydro-1,5-methano-pyrido[1,2a][1,5]diazocin-8-one;  
9-cyano-1,2,3,4,5,6-hexahydro-1,5-methano-pyrido[1,2a][1,5]diazocin-8-one;  
9-ethynyl-1,2,3,4,5,6-hexahydro-1,5-methano-pyrido[1,2a][1,5]diazocin-8-one;  
9-(2-propenyl)-1,2,3,4,5,6-hexahydro-1,5-methano-pyrido[1,2a][1,5]diazocin-8-one;  
9-(2-propyl)- 1,2,3,4,5,6-hexahydro-1,5-methano-pyrido[1,2a][1,5]diazocin-8-one;  
9-carbomethoxy-1,2,3,4,5,6-hexahydro-1,5-methano-pyrido[1,2a][1,5]diazocin-8-one;  
9-carboxyaldehyde-1,2,3,4,5,6-hexahydro-1,5-methano-pyrido[1,2a][1,5]diazocin-8-one;  
9-(2,6-difluorophenyl)-1,2,3,4,5,6-hexahydro-1,5-methano-pyrido[1,2a][1,5]diazocin-8-one;  
9-phenyl-1,2,3,4,5,6-hexahydro-1,5-methano-pyrido[1,2a][1,5]diazocin-8-one;  
9-(2-fluorophenyl)-1,2,3,4,5,6-hexahydro-1,5-methano-pyrido[1,2a][1,5]diazocin-8-one;  
9-(4-fluorophenyl)-1,2,3,4,5,6-hexahydro-1,5-methano-pyrido[1,2a][1,5]diazocin-8-one;  
9-(3-fluorophenyl)-1,2,3,4,5,6-hexahydro-1,5-methano-pyrido[1,2a][1,5]diazocin-8-one;  
9-(3,5-difluorophenyl)-1,2,3,4,5,6-hexahydro-1,5-methano-pyrido[1,2a][1,5]diazocin-8-one;

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9-(2,4-difluorophenyl)-1,2,3,4,5,6-hexahydro-1,5-methano-  
pyrido[1,2a][1,5]diazocin-8-one;

9-(2,5-difluorophenyl)-1,2,3,4,5,6-hexahydro-1,5-methano-  
pyrido[1,2a][1,5]diazocin-8-one;

6-methyl-5-oxo-6,13-diazatetracyclo[9.3.1.0<sup>2,10</sup>.0<sup>4,8</sup>]pentadeca-2(10),3,8-triene;

5-oxo-6,13-diazatetracyclo[9.3.1.0<sup>2,10</sup>.0<sup>4,8</sup>]pentadeca-2(10),3,8-triene;

6-oxo-5,7,13-triazatetracyclo[9.3.1.0<sup>2,10</sup>.0<sup>4,8</sup>]pentadeca-2(10),3,8-triene;

4,5-difluoro-10-aza-tricyclo[6.3.1.0<sup>2,7</sup>]dodeca-2(7),3,5-triene;

5-fluoro-10-aza-tricyclo[6.3.1.0<sup>2,7</sup>]dodeca-2(7),3,5-triene-4-carbonitrile;

4-ethynyl-5-fluoro-10-aza-tricyclo[6.3.1.0<sup>2,7</sup>]dodeca-2(7),3,5-triene;

5-ethynyl-10-aza-tricyclo[6.3.1.0<sup>2,7</sup>]dodeca-2(7),3,5-triene-4-carbonitrile;

6-methyl-5-thia-5-dioxa-6,13-diazatetracyclo[9.3.1.0<sup>2,10</sup>.0<sup>4,8</sup>]pentadeca-2(10),3,8-  
triene;

10-aza-tricyclo[6.3.1.0<sup>2,7</sup>]dodeca-2(7),3,5-triene;

4-fluoro-10-aza-tricyclo[6.3.1.0<sup>2,7</sup>]dodeca-2(7),3,5-triene;

4-methyl-10-aza-tricyclo[6.3.1.0<sup>2,7</sup>]dodeca-2(7),3,5-triene;

4-trifluoromethyl-10-aza-tricyclo[6.3.1.0<sup>2,7</sup>]dodeca-2(7),3,5-triene;

4-nitro-10-azatricyclo[6.3.1.0<sup>2,7</sup>]dodeca-2(7),3,5-triene;

7-methyl-5,7,13-triazatetracyclo[9.3.1.0<sup>2,10</sup>.0<sup>4,8</sup>]pentadeca-2(10),3,5,8-tetraene;

6-methyl-5,7,13-triazatetracyclo[9.3.1.0<sup>2,10</sup>.0<sup>4,8</sup>]pentadeca-2(10),3,5,8-tetraene;

6,7-dimethyl-5,7,13-triazatetracyclo[9.3.1.0<sup>2,10</sup>.0<sup>4,8</sup>]pentadeca-2(10),3,5,8-  
tetraene;

6-methyl-7-phenyl-5,7,13-triazatetracyclo[9.3.1.0<sup>2,10</sup>.0<sup>4,8</sup>]pentadeca-2(10),3,5,8-  
tetraene;

6,7-dimethyl-5,8,14-triazatetracyclo[10.3.1.0<sup>2,11</sup>.0<sup>4,9</sup>]hexadeca-2(11),3,5,7,9-  
pentaene;

5,8,14-triazatetracyclo[10.3.1.0<sup>2,11</sup>.0<sup>4,9</sup>]hexadeca-2(11),3,5,7,9-pentaene;

14-methyl-5,8,14-triazatetracyclo[10.3.1.0<sup>2,11</sup>.0<sup>4,9</sup>]hexadeca-2(11),3,5,7,9-  
pentaene;

5-oxa-7,13-diazatetracyclo[9.3.1.0<sup>2,10</sup>.0<sup>4,8</sup>]pentadeca-2(10),3,6,8-tetraene;

6-methyl-5-oxa-7,13-diazatetracyclo[9.3.1.0<sup>2,10</sup>.0<sup>4,8</sup>]pentadeca-2(10),3,6,8-  
tetraene;

4-chloro-10-azatricyclo[6.3.1.0<sup>2,7</sup>]dodeca-2(7),3,5-triene;

10-azatricyclo[6.3.1.0<sup>2,7</sup>]dodeca-2(7),3,5-trien-4-yl cyanide;

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1-(10-azatricyclo[6.3.1.0<sup>2,7</sup>]dodeca-2(7),3,5-trien-4-yl)-1-ethanone;  
10-azatricyclo[6.3.1.0<sup>2,7</sup>]dodeca-2(7),3,5-trien-4-ol;  
7-methyl-5-oxa-6,13-diazatetracyclo[9.3.1.0<sup>2,10</sup>.0<sup>4,8</sup>]pentadeca-2,4(8),6,9-tetraene;  
4,5-dichloro-10-azatricyclo[6.3.1.0<sup>2,7</sup>]dodeca-2(7),3,5-triene;  
11-azatricyclo[7.3.1.0<sup>2,7</sup>]trideca-2(7),3,5-triene-5-carbonitrile;  
1-[11-azatricyclo[7.3.1.0<sup>2,7</sup>]trideca-2(7),3,5-trien-5-yl]-1-ethanone;  
1-[11-azatricyclo[7.3.1.0<sup>2,7</sup>]trideca-2(7),3,5-trien-5-yl]-1-propanone;  
4-fluoro-11-azatricyclo[7.3.1.0<sup>2,7</sup>]trideca-2(7),3,5-triene-5-carbonitrile;  
5-fluoro-11-azatricyclo[7.3.1.0<sup>2,7</sup>]trideca-2(7),3,5-triene-4-carbonitrile;  
6-methyl-7-thia-5,14-diazatetracyclo[10.3.1.0<sup>2,10</sup>.0<sup>4,8</sup>]hexadeca-2(10),3,5,8-tetraene;  
6-methyl-5,7,14-triazatetracyclo[10.3.1.0<sup>2,10</sup>.0<sup>4,8</sup>]hexadeca-2(10),3,5,8-tetraene;  
6,7-dimethyl-5,7,14-triazatetracyclo[10.3.1.0<sup>2,10</sup>.0<sup>4,8</sup>]hexadeca-2(10),3,5,8-tetraene;  
5,7,14-triazatetracyclo[10.3.1.0<sup>2,10</sup>.0<sup>4,8</sup>]hexadeca-2(10),3,5,8-tetraene;  
5,6-dimethyl-5,7,14-triazatetracyclo[10.3.1.0<sup>2,10</sup>.0<sup>4,8</sup>]hexadeca-2(10),3,6,8-tetraene;  
5-methyl-5,7,14-triazatetracyclo[10.3.1.0<sup>2,10</sup>.0<sup>4,8</sup>]hexadeca-2(10),3,6,8-tetraene;  
6-(trifluoromethyl)-7-thia-5,14-diazatetracyclo[10.3.1.0<sup>2,10</sup>.0<sup>4,8</sup>]hexadeca-2(10),3,5,8-tetraene;  
5,8,15-triazatetracyclo[11.3.1.0<sup>2,11</sup>.0<sup>4,9</sup>]heptadeca-2(11),3,5,7,9-pentaene;  
7-methyl-5,8,15-triazatetracyclo[11.3.1.0<sup>2,11</sup>.0<sup>4,9</sup>]heptadeca-2(11),3,5,7,9-pentaene;  
6-methyl-5,8,15-triazatetracyclo[11.3.1.0<sup>2,11</sup>.0<sup>4,9</sup>]heptadeca-2(11),3,5,7,9-pentaene;  
6,7-dimethyl-5,8,15-triazatetracyclo[11.3.1.0<sup>2,11</sup>.0<sup>4,9</sup>]heptadeca-2(11),3,5,7,9-pentaene;  
7-oxa-5,14-diazatetracyclo[10.3.1.0<sup>2,10</sup>.0<sup>4,8</sup>]hexadeca-2(10),3,5,8-tetraene;  
6-methyl-7-oxa-5,14-diazatetracyclo[10.3.1.0<sup>2,10</sup>.0<sup>4,8</sup>]hexadeca-2(10),3,5,8-tetraene;  
5-methyl-7-oxa-6,14-diazatetracyclo[10.3.1.0<sup>2,10</sup>.0<sup>4,8</sup>]hexadeca-2(10),3,5,8-tetraene;

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6-methyl-5-oxa-7,14-diazatetracyclo[10.3.1.0<sup>2,10</sup>.0<sup>4,8</sup>]hexadeca-2(10),3,6,8-tetraene;

7-methyl-5-oxa-6,14-diazatetracyclo[10.3.1.0<sup>2,10</sup>.0<sup>4,8</sup>]hexadeca-2(10),3,6,8-tetraene;

4,5-difluoro-11-azatricyclo[7.3.1.0<sup>2,7</sup>]trideca-2(7),3,5-triene;

4-chloro-5-fluoro-11-azatricyclo[7.3.1.0<sup>2,7</sup>]trideca-2(7),3,5-triene;

5-chloro-4-fluoro-11-azatricyclo[7.3.1.0<sup>2,7</sup>]trideca-2(7),3,5-triene;

4-(1-ethynyl)-5-fluoro-11-azatricyclo[7.3.1.0<sup>2,7</sup>]trideca-2(7),3,5-triene;

5-(1-ethynyl)-4-fluoro-11-azatricyclo[7.3.1.0<sup>2,7</sup>]trideca-2(7),3,5-triene;

5,6-difluoro-11-aza-tricyclo[7.3.1.0<sup>2,7</sup>]trideca-2,4,6-triene;

6-trifluoromethyl-11-aza-tricyclo[7.3.1.0<sup>2,7</sup>]trideca-2,4,6-triene;

6-methoxy-11-aza-tricyclo[7.3.1.0<sup>2,7</sup>]trideca-2(7),3,5-triene;

11-aza-tricyclo[7.3.1.0<sup>2,7</sup>]trideca-2(7),3,5-trien-6-ol;

6-fluoro-11-aza-tricyclo[7.3.1.0<sup>2,7</sup>]trideca-2(7),3,5-triene;

11-aza-tricyclo[7.3.1.0<sup>2,7</sup>]trideca-2(7),3,5-trien-5-ol;

4-nitro-11-aza-tricyclo[7.3.1.0<sup>2,7</sup>]trideca-2(7),3,5-triene;

5-nitro-11-aza-tricyclo[7.3.1.0<sup>2,7</sup>]trideca-2(7),3,5-triene;

5-fluoro-11-aza-tricyclo[7.3.1.0<sup>2,7</sup>]trideca-2(7),3,5-triene; and

6-hydroxy-5-methoxy-11-aza-tricyclo[7.3.1.0<sup>2,7</sup>]trideca-2(7),3,5-triene and

their pharmaceutically acceptable salts and their optical isomers.

11. (original) The pharmaceutical composition of claim 1, in which the NRPA is selected from the group consisting of:

9-bromo-1,2,3,4,5,6-hexahydro-1,5-methano-pyrido[1,2-a][1,5]diazocin-8-one;

9-chloro-1,2,3,4,5,6-hexahydro-1,5-methano-pyrido[1,2-a][1,5]diazocin-8-one;

9-flouro-1,2,3,4,5,6-hexahydro-1,5-methano-pyrido[1,2-a][1,5]diazocin-8-one;

9-acetyl-1,2,3,4,5,6-hexahydro-1,5-methano-pyrido[1,2-a][1,5]diazocin-8-one;

9-iodo-1,2,3,4,5,6-hexahydro-1,5-methano-pyrido[1,2-a][1,5]diazocin-8-one;

9-cyano-1,2,3,4,5,6-hexahydro-1,5-methano-pyrido[1,2-a][1,5]diazocin-8-one;

9-carbomethoxy-1,2,3,4,5,6-hexahydro-1,5-methano-pyrido[1,2a][1,5]diazocin-8-one;

9-carboxyaldehyde-1,2,3,4,5,6-hexahydro-1,5-methano-pyrido[1,2a][1,5]diazocin-8-one;

9-(2,6-difluorophenyl)-1,2,3,4,5,6-hexahydro-1,5-methano-pyrido[1,2a][1,5]diazocin-8-one;

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9-phenyl-1,2,3,4,5,6-hexahydro-1,5-methano-pyrido[1,2a][1,5]diazocin-8-one;  
9-(2-fluorophenyl)-1,2,3,4,5,6-hexahydro-1,5-methano-pyrido[1,2a][1,5]diazocin-8-one;  
6-methyl-5-thia-5-dioxa-6,13-diazatetracyclo[9.3.1.0<sup>2,10</sup>.0<sup>4,8</sup>]pentadeca-2(10),3,8-triene;  
4-fluoro-10-aza-tricyclo[6.3.1.0<sup>2,7</sup>]dodeca-2(7),3,5-triene;  
4-trifluoromethyl-10-aza-tricyclo[6.3.1.0<sup>2,7</sup>]dodeca-2(7),3,5-triene;  
4-nitro-10-azatricyclo[6.3.1.0<sup>2,7</sup>]dodeca-2(7),3,5-triene;  
6-methyl-5,7,13-triazatetracyclo[9.3.1.0<sup>2,10</sup>.0<sup>4,8</sup>]pentadeca-2(10),3,5,8-tetraene;  
6,7-dimethyl-5,8,14-triazatetracyclo[10.3.1.0<sup>2,11</sup>.0<sup>4,9</sup>]hexadeca-2(11),3,5,7,9-pentaene;  
5,8,14-triazatetracyclo[10.3.1.0<sup>2,11</sup>.0<sup>4,9</sup>]hexadeca-2(11),3,5,7,9-pentaene;  
5-oxa-7,13-diazatetracyclo[9.3.1.0<sup>2,10</sup>.0<sup>4,8</sup>]pentadeca-2(10),3,6,8-tetraene;  
6-methyl-5-oxa-7,13-diazatetracyclo[9.3.1.0<sup>2,10</sup>.0<sup>4,8</sup>]pentadeca-2(10),3,6,8-tetraene;  
10-azatricyclo[6.3.1.0<sup>2,7</sup>]dodeca-2(7),3,5-trien-4-yl cyanide;  
1-(10-azatricyclo[6.3.1.0<sup>2,7</sup>]dodeca-2(7),3,5-trien-4-yl)-1-ethanone;  
11-azatricyclo[7.3.1.0<sup>2,7</sup>]trideca-2(7),3,5-triene-5-carbonitrile;  
1-[11-azatricyclo[7.3.1.0<sup>2,7</sup>]trideca-2(7),3,5-trien-5-yl]-1-ethanone;  
1-[11-azatricyclo[7.3.1.0<sup>2,7</sup>]trideca-2(7),3,5-trien-5-yl]-1-propanone;  
4-fluoro-11-azatricyclo[7.3.1.0<sup>2,7</sup>]trideca-2(7),3,5-triene-5-carbonitrile;  
5-fluoro-11-azatricyclo[7.3.1.0<sup>2,7</sup>]trideca-2(7),3,5-triene-4-carbonitrile;  
6-methyl-7-thia-5,14-diazatetracyclo[10.3.1.0<sup>2,10</sup>.0<sup>4,8</sup>]hexadeca-2(10),3,5,8-tetraene;  
6-methyl-5,7,14-triazatetracyclo[10.3.1.0<sup>2,10</sup>.0<sup>4,8</sup>]hexadeca-2(10),3,5,8-tetraene;  
6,7-dimethyl-5,7,14-triazatetracyclo[10.3.1.0<sup>2,10</sup>.0<sup>4,8</sup>]hexadeca-2(10),3,5,8-tetraene;  
6-methyl-7-oxa-5,14-diazatetracyclo[10.3.1.0<sup>2,10</sup>.0<sup>4,8</sup>]hexadeca-2(10),3,5,8-tetraene;  
6-methyl-5-oxa-7,14-diazatetracyclo[10.3.1.0<sup>2,10</sup>.0<sup>4,8</sup>]hexadeca-2(10),3,6,8-tetraene;  
5,6-difluoro-11-aza-tricyclo[7.3.1.0<sup>2,7</sup>]trideca-2,4,6-triene;  
6-trifluoromethyl-11-aza-tricyclo[7.3.1.0<sup>2,7</sup>]trideca-2,4,6-triene;  
6-methoxy-11-aza-tricyclo[7.3.1.0<sup>2,7</sup>]trideca-2(7),3,5-triene;

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6-fluoro-11-aza-tricyclo[7.3.1.0<sup>2,7</sup>]trideca-2(7),3,5-triene; and  
11-aza-tricyclo[7.3.1.0<sup>2,7</sup>]trideca-2(7),3,5-trien-5-ol and  
their pharmaceutically acceptable salts and their optical isomers.

12. (original) The pharmaceutical composition of claim 1, wherein the GABA<sub>A</sub> inverse agonist is N-Benzyl-6-ethoxy-4-oxo-1,5-naphthyridine-3-carboxamide, or a prodrug thereof, or a pharmaceutically acceptable salt or solvate of said compound or prodrug.

Claims 13. - 16. (withdrawn and canceled)

17. (new) The pharmaceutical composition of claim 3 wherein the GABA<sub>A</sub> inverse agonist has a functional efficacy at the  $\alpha 1$  and/or  $\alpha 5$  receptor subtypes of less than -10%.

18. (new) The pharmaceutical composition of claim 3 wherein the efficacy measured at the  $\alpha 2$  and  $\alpha 3$  receptor subtypes is greater than 10%.

19. (new) The pharmaceutical composition of claim 3, wherein the GABA<sub>A</sub> inverse agonist has functional potency (EC<sub>50</sub> values) at the  $\alpha 1$  and/or  $\alpha 5$  receptor subtypes of less than 150 nM.

20. (new) The pharmaceutical composition of claim 3, wherein the GABA<sub>A</sub> inverse agonist has a functional efficacy at the  $\alpha 5$  receptor subtype of less than -10%, and the efficacy measured at the  $\alpha 1$ ,  $\alpha 2$  and  $\alpha 3$  receptor subtypes is greater than 10%.

21. (new) The pharmaceutical composition of claim 5 wherein the GABA<sub>A</sub> inverse agonist has a functional potency (EC<sub>50</sub> values) at the  $\alpha 5$  receptor subtype of less than 150 nM.

22. (new) The pharmaceutical composition of claim 3 wherein the GABA<sub>A</sub> inverse agonist at the  $\alpha 1$  and/or  $\alpha 5$  receptor subtypes has a binding K<sub>i</sub> of less than 30 nM.

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